## REMARKS

Claims 35-39 are pending.

The rejection under 35 U.S.C. §103(a)

Claims 35-39 remain rejected as being obvious over WO 99/58478 (Claus) and WO 94/11337 (Arne).

The Applicants respectfully request reconsideration and withdrawal of this rejection. The major flaw in this rejection is the purported motivation cited for producing a low salt compound. According to the Office Action, motivation to produce a low salt compound arises because there is an expectation that decreasing the salt content would decrease side effects and undesirable properties. See the Office Action, page 3:

One of ordinary skill in the art would be motivated to optimize the purity of the isolated product, lowering the salt content to less than 10% by weight, through routine and normal experimentation, with the reasonable expectation that a decrease in salt impurities would decrease side-effects and undesirable pharmacokinetic properties.

This argument is mistaken in general, i.e., when applied to compounds useful for pharmaceutical purposes in general. It is also mistaken in particular, i.e., when applied to the particular class of compounds being claimed.

In general, it is well know that there is no expectation that salts of pharmaceutical compounds are undesirable in terms of either side effects or other properties. In fact, it is so well known as to need no citations to evidence that thousands of pharmaceutical compounds are used effectively as salts of one form or another.

In particular, as applied to the compounds being claimed, and as explained in the previous Amendment, the prior art taught that compounds of the type being claimed should be used in the form of salts. In the previous Amendment, the Applicants pointed out that this teaching of the prior art in U.S. Patent No. 6,858,650 that compounds of the type being claimed should be used in the form of salts is a teaching away from the claimed invention and is strong evidence that the claimed invention is non-obvious. The Office Action cited Arne (page 6, line 37) and Claus (page 35, third paragraph, first two lines) as purportedly negating the impact of this teaching away.

The Applicants do not agree that Arne and Claus outweigh the teachings of U.S.

Patent No. 6,858,650. The disclosures in Arne and Claus are mere "boilerplate" and would be understood as such by those skilled in the art. That is, Arne and Claus did not give serious consideration to whether the compound should be in the free base or the salt form but instead merely recited the free base along with salts as theoretical possibilities. In contrast, U.S.

Patent No. 6,858,650 (priority application filed 1999) reflects work done after Arne (published in 1994) and Claus (priority application filed 1998) which looked more carefully at the issue of free base versus salts. The extensive treatment that U.S. Patent No. 6,858,650 gave to this issue is detailed in the previous Amendment. In view of these considerations, U.S. Patent No. 6,858,650 should be accorded greater weight on this issue than Arne or Claus.

Arme did not provide any motivation to reduce salt content. Instead, Arme taught that salts are desirable. Arme taught the transformation of compounds into mandelate salts (see page 13, line 16 to page 14, line 19). Furthermore, the pharmacological tests in Arme were done using salts (see page 14, lines 20-33).

Thus, there was no motivation to reduce the salt content of the claimed compounds to the recited level of less than 10% by weight.

Moreover, the Applicants continue to believe that the claimed invention shows unexpected results for the reasons given in the previous Amendment. The Office Action did not agree with this position. According to the Office Action, a comparison has not been made with the closest prior art. The Office Action argued that the closest prior art is the hydrochloride salt disclosed in Arne rather than the fumarate salt used in the Applicants' comparison.

The Applicants believe the Office Action is mistaken. The fumarate salts used by the Applicants are compounds that, except for their salt content, fall within the scope of the structural formula recited in present claim 35. The hydrochloride salts disclosed in Arne are compounds that, even ignoring their salt content, fall outside the scope of the structural formula recited in present claim 35.

See page 1, lines 18-27, of Arne, where the structure of formula I and the definition of R<sup>1</sup> mean that the compounds of Arne cannot satisfy the structural formula recited in the present claims. There is no possibility in Arne for the presence of the carbonyl group attached to the R group in the structural formula recited in present claim 35.

It should go without saying that the closest prior art should be a compound that has the same chemical structure as the claimed compound. Thus, the Applicants' fumarate salts, since they have a structure within the scope of the structural formula recited in present claim 35, are closer than Arne's hydrochloride salts, which have a structure outside the scope of the structural formula recited in present claim 35.

Attorney Docket No. 12961/46601

U.S. Patent Application Serial No. 10/532,836

In view of the above, it is respectfully requested that this rejection be withdrawn.

The time for responding to the Office Action was set for July 4, 2008. Therefore, it is believed that this response is timely. If this is in error, please treat this response as containing a Petition for the Extension of Time under 37 C.F.R. § 1.136(a) for a period sufficient to permit the filing of this paper and charge any corresponding fees to Kenyon & Kenyon's

The Applicants hereby make a Conditional Petition for any relief available to correct any defect seen in connection with the filing of this paper, or any defect seen to be remaining in this application after the filing of this paper. The Commissioner is authorized to charge Kenyon & Kenyon's Deposit Account No. 11-0600 for the Petition fee and any other fees required to effect this Conditional Petition.

Respectfully Submitted,

Date: JULY

JULY 7, 2008

Deposit Account No. 11-0600.

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